I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
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Baxter

ORIG AMENDMENT: SU

ORIGINAL

February 19, 1999

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Metabolic and Endocrine
Drug Products
Central Document Room 14B-19
5600 Fishers Lane - HFD-510
Rockville, MD 20857-1706

REVIEWS COMPL...
CSO ACTION:
☐ LETTER ☒ ...
/S/ [redacted]
CSO INITIALS 3/17/99

Re: NDA 20-924: Cernevit™-12 IV Multivitamins

Clarification of Safety Update Information

-- MINOR AMENDMENT --

Noted [redacted] 3/17/99

Dear Sir or Madam:

On February 8, 1999, Baxter received a verbal request for clarification of the following three German terms used in Case No. 7 of the January 13, 1999 Safety Update submitted to the above-referenced file:

> bladders dorsal;
> Mundschleimhauterosionen; and
> finespotty exanthema conjunctivitis.

The sponsor has responded adequately to the deficiencies to the Jan 13, 1999 safety update /S/ [redacted]

Baxter's response to this request was provided on February 17, 1999 by Dr. John Wesley of Baxter during a telephone conversation with Dr. Jean Temeck of the Division. This letter provides a summary of their conversation.

Dr. Wesley defined "bladders dorsal" as similar to epidurmolysis bullosa (an exfoliating skin lesion forming blisters) over the skin in the backbone area. The second term, Mundschleimhauterosionen, literally means open sores or erosions of the lips and oral mucosa. The last term, finespotty exanthema conjunctivitis is an allergic-type inflammation or eruption of the conjunctiva. Drs. Wesley and Temeck discussed these terms and their meanings in some detail during their conversation. Following their discussion, Dr. Temeck

Baxter

indicated she had sufficient information regarding the terms used in the German case report.

Thank you for incorporating this information into the file. If you have questions or comments, please contact Ms. Linda Coleman or Tamima Itani, Ph.D. at (847) 270-2577.

Sincerely,

Marcia Marconi (Lc)

Marcia Marconi
Vice President, Regulatory Affairs
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5600 Fishers Lane - HFD-510
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REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

Re: NDA 20-924: Cernevit™-12 IV Multivitamins

Safety Update

-- MINOR AMENDMENT --

Dear Sir or Madam:

Item 9 (Safety Update) of the original NDA submitted to the Agency on March 20, 1998 included six reports of adverse events received by Baxter between April, 1988 and January, 1998 from worldwide pharmacovigilance. Since January, 1998, there have been three additional events reported worldwide. A summary of these three events follows. From January, 1998 to the present, 4 million vials of Cernevit® Multivitamin Preparation[1] have been sold worldwide.

Case 7: 5/98

This case was reported in Germany; therefore, the drug names and diagnosis may be different from terminology used in the U.S. A 71 year old female was admitted to the hospital on 5/2/98 in a coma with an elevated temperature (40°C), tetraparesis and pancreatitis. She was diagnosed on 5/3/98 with a cervical lymphome and no hope of survival. The patient was started on

Have to call sponsor for correct medical terminology for the following terms: "bladders dorsal", "Mundschleimhautläsionen", "exanthema conjunctivitis"

/S/ [redacted]

2/8/99

[1] Cernevit® Multivitamin Preparation is the brand name of the "Cernevit" product which is currently marketed by Baxter worldwide. Cernevit™-12 IV Multivitamins is the brand name of the "Cernevit" product which will be marketed in the United States under this NDA.

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parenteral nutrition on 5/4/98, which included one vial of Cernevit® Multivitamin Preparation per day. Co-morbidities identified by 5/8 included sepsis, pancreatitis, tetraparesis, leucopenia, edema of the lips, and suspicion of mycotic pneumonia. Parenteral nutrition including Cernevit® was discontinued on 5/10/98. On 5/10, she developed "bladders dorsal" (skin bubbles on the back and backbone area), on 5/12 she developed Mundschleimhauterosionen (described as erosions of the oral mucosa and lips), and on 5/13, finespotty exanthema conjunctivitis. Concurrent medications included: Noctamid (Lormetazepam), Dexium (Calciumdobesilat), Saroten (Amitryptilin), Moduretik (Amilorid, Hydrochlorothiazid), Zovirax (Aciclovir), Heparin, Sterofundin, Ben-u-ron suppositories (Paracetamol), Novalgin (Metamizol), Lasix (Furosemide), Zienam (Imipenem, Cilastatin), Insulin, Arterenol (Norepinephrin), Dopamin, Dormicum (Midazolam), Sodium Bicarbonate, Potassium Chloride, Sodium Chloride, Human Albumin, Intralip, Glucose, Dobutrex (Dobutamin), Etomidat, Aminomix, Atenativ (Antithrombin III), Fentanyl, Thrombocytes, Erythrocytes, Vancomycin, Meronem (Dexamethason), Zyloric (Allopurinol), Haes, Sostril (Ranitidin), Methotrexat, Alexan (Cytarabin), Fresh frozen plasma, Digimerck (Digitoxin), Dipeptamin (L-Alanyl-L-Glutamin), Thomaemin, Neupogen (Filgastrim), Pentacarinat (Pentamidin) and Amphotericin B. The patient died on 5/14/98.

Case 8: 8/98

This case was reported in the United Kingdom. A male patient in his twenties was receiving long term TPN therapy for the treatment of either short bowel syndrome or intestinal failure (exact diagnosis not disclosed). In March, 1998, the vitamin additive was changed to Cernevit®. Since that time, the patient noticed an increase in hair growth, particularly on the arms and legs, and a darkening of the hair color.

Case 9: 11/98

This case was reported in the United States. A female patient suffering from hyperemesis was treated at home with hydration solution containing one vial of Cernevit®. The patient developed a rash on the forearm only. Concurrent medications included phenergan suppositories. The rash began to clear following the completion of the Cernevit® containing hydration solution. The patient received one vial of Cernevit® and was not re-exposed.

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Thank you for incorporating this safety update into the file. If you have questions or comments, please contact Ms. Linda Coleman or Tamima Itani, Ph.D. at (847) 270-2577.

Sincerely,

Marcia Marconi (RC)

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